

directed to the subject matter thereof. Thus, claims 1-7 and 9-20 are pending. The specification as originally filed contains support for the amendments. No new matter is added.

The Abstract was objected to. Although Applicants respectfully disagree with the basis for objection provided in the Action, Applicants have amended the Abstract to provide a structural representation for the compounds. Contrary to the Office's position in the Action, the Abstract provides a use for the compounds. Applicants respectfully request reconsideration and withdrawal of the objection.

The specification was objected to. Applicants amend the specification on pages 2 and 3, inserting page numbers for corresponding journal citations. Reconsideration and withdrawal of the objection are respectfully requested.

Applicants traverse the Office's objection to Figures 2-6. These figures contain data obtained in the models of predictive *in vitro* assays (e.g., in blood and liver homogenate). Within the limits of laboratory investigations, upon addition of all agents, enzymatic hydrolysis was measured as soon as possible. Because experimental conditions vary, and enzymatic hydrolysis is rapid in these predictive systems, time = 0 corresponds to the initial measurement and was taken as soon as possible after all reagents were added. Furthermore, these models are not isolated enzyme studies. There are various other uncharacterized metabolic events which contribute to the data presented. For example, enzymes present in the homogenate are likely acting on substrate 1-(5-(R)-hydroxyhexyl)-3,7-dimethylxanthine ("lisofylline"), chemically altering it and resulting in a change in percent hydrolysis reported over time.

These data would be interpreted by skilled artisans, in view of the experimental protocols described in examples 21-25. Applicants respectfully submit that the Office has failed to fully consider these data in context with the intent of the studies and the knowledge of skilled artisans in this field. Reconsideration and withdrawal of the objection are respectfully requested.

Claims 1-19 were rejected jointly under 35 USC §112, first paragraph, and 35 USC §101. Applicants respectfully traverse this rejection.

Prodrugs need not be structurally identical. In fact much of the skill in this art is identifying structural variants which will withstand "first pass effect" (see specification, page 2, lines 22-32, in particular). The claimed compounds intentionally have selectively different hydrolytic potentials for just this reason. The claimed compounds are partially or entirely converted to lisofylline, which Applicants have disclosed is useful in various therapeutic applications. The specification does indeed disclose therapeutic utilities for lisofylline and discloses and incorporates by reference, the corresponding US application claiming, *inter alia*, a pharmaceutical composition of lisofylline, which illustrates efficacy of the compound lisofylline.

Unfortunately, the Office has misread Applicants' specification. The two dosages provided on page 9, 0.1 to 1000 mg/kg and 0.0001 to 40 mg/kg are a *daily* and *single administration* doses, as clearly stated in the specification. These ranges are not "impossibly" broad.

Applicants respectfully submit that this rejection is improper, particularly in view of Applicants' amendments, and thus, they request reconsideration and withdrawal of the rejection.

Claims 1-8, 10, 11, 15-17 and 19 were rejected under 35 USC §102(b) over published PCT application no. WO 93/17864 and claims 1-4, 6-8 and 10 were rejected under 35 USC §102(b) over European patent application no. 286,041. Applicants respectfully submit that the above amendments overcome these rejections and thus request reconsideration and withdrawal of the rejection.

The Action independently rejected claims 1-4, 6-8, 10, 15 and 16 and claims 1-8 and 1-19 over claims 1-20 of US serial no. 08/306,091 and claims 1, 26 and 27 of US serial no. 08/199,368, respectively. As no claims have issued in either of the parent applications or in the instant applications, Applicants will accordingly manage the subject matter of these three applications.

Applicants traverse the rejection of claims 1-19 under 35 USC §112, first and second paragraphs. This rejection provides 29 enumerated points. Applicants amendments have

addressed these points, either obviating or overcoming the specific objections. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

In view of the foregoing amendments and remarks, the application is in condition for allowance. Applicants respectfully solicit favorable consideration and entry of the amendments and prompt issuance of a Notice of Allowance directed to claims 1-7 and 9-20.

Should the Examiner deem that Applicants' further action would place the application in even better condition for allowance, Applicants' undersigned representative respectfully requests that Examiner Berch telephone him at the number set forth below.

Please grant any extension of time deemed necessary for entry of this communication. Please charge any deficient fees or credit any overpayment to Deposit Account No. 03-1182.

Respectfully submitted,



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